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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,529	10/24/2003	Wei Liu	WYE-010	1341

54623 7590 12/14/2005

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,529	WEI LIU	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-23 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-23 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7 and 14, drawn to an isolated polynucleotide comprising a nucleic acid sequence encoding SEQ ID NO:2 and having calcineurin phosphodiesterase function and a host cell comprising said polynucleotide, classified in class 536, 435subclass 23.1;325.

II. Claims 8-11, drawn to an isolated polypeptide fragment comprising a fragment of SEQ ID NO:2, classified in class 530, subclass 350.

III. Claims 12-13, drawn to an antibody capable of binding to SEQ ID NO:2 and a kit comprising said antibody, classified in class 530, subclass 387.9.

IV. Claim 15, drawn to a transgenic non-human animal comprising a polynucleotide comprising a nucleic acid sequence encoding SEQ ID NO:2 and having calcineurin phosphodiesterase function, classified in class 800, subclass 8.

V. Claim 16, drawn to a non-human animal wherein at least one allele of a gene in the genome is functionally disrupted wherein said gene encodes a polypeptide that has at least 70% identity to SEQ ID NO:2 , classified in class 800, subclass 8.

VI. Claim 17, drawn to an in vitro method of identifying an agent capable of binding CLPP1 using an agent and a CLPP1 polypeptide and detecting binding, classified in class 435, subclass 7.1.

VII. Claim 18, drawn to an in vitro method of identifying an agent capable of modulating CLPP1 activity fusing an agent and a CLPP1 polypeptide and detecting activity, classified in class 435, subclass 4.

VIII. Claims 19 and 20, drawn to a pharmaceutical comprising an agent that modulates CLPP1 and a method of treating disease using the pharmaceutical, unclassifiable.

IX. Claims 21-23, drawn to a polynucleotide capable of inhibiting CLPP1 expression and a method of using said polynucleotide, classified in class 536, subclass 24.5.

The inventions are distinct, each from the other because of the following reasons:

The polynucleotide of Invention I is patentably distinct from the polypeptide of Invention II. The polynucleotide encodes the polypeptide. Polypeptides are composed of amino acids and polynucleotides are composed of purines and pyrimidines, and therefore, the polypeptides and polynucleotides are structurally distinct. Any relationship between a polynucleotide and a polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, the polynucleotide of Invention I does not necessarily encode the isolated polypeptides of Invention II. The information provided by the polynucleotide can be used to make different polypeptides. Furthermore, the isolated polypeptide can be recovered from a natural source using antibodies or affinity chromatography, not requiring the polynucleotide of Invention I. Searching Inventions I and II together would be a search burden because the searches are not coextensive. The Inventions have a separate status in the art as shown by their different classifications.

The polynucleotide of Invention I is unrelated to the antibody of Invention III. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04,

MPEP § 808.01). In the instant case the polynucleotides of Invention I is not used with the antibody of Invention II. The Inventions are classified differently. It would require undue burden to search the polynucleotide with the antibody.

The polynucleotide of Invention I and the transgenic animals of each of Inventions IV and V are patentably distinct. The polynucleotide and the animal are functionally and structurally distinct and have different purpose and different modes of action. The polynucleotide of Invention I can be used in vitro to make protein or as a probe. The animals of Inventions IV and V can be used to screen test compounds. The inventions are classified differently. It would require an undue burden to search Invention I with either of Inventions IV or V.

The polynucleotide of Invention I is patentably distinct from the methods of either of Inventions VI or VII. In the instant case the polynucleotide of Invention I is not used with the method of Invention VI. The methods of Invention VI and VII require a polypeptide, which does not require the polynucleotide of Invention I. The polynucleotide operates by encoding a polypeptide whereas the methods assay for binding with a polypeptide or altered activity of a polypeptide. The Inventions are classified differently. It would require undue burden to search the polynucleotide with the methods of using a polypeptide.

The polynucleotide of Invention I is patentably distinct from the pharmaceutical of Invention VIII. In the instant case the polynucleotide of Invention I is structurally and functionally distinct from the pharmaceutical comprising a functional regulator of a CLPP1 polypeptide. The isolated polynucleotide and the pharmaceutical are not used together. The polynucleotide operates by encoding a polypeptide whereas the pharmaceutical operates by

modulating CLPP1 activity. The Inventions are classified differently. It would require undue burden to search the polynucleotide with the pharmaceutical.

The polynucleotide of Invention I and that of Invention IX are patentably distinct. The polynucleotide of Invention I encodes a CLPP1 polypeptide. The polynucleotide of Invention IX inhibits CLPP1. The structure, function and mode of action of the two polynucleotides are different. It would require undue burden to search the polynucleotide encoding a CLPP1 polypeptide with the polynucleotide capable of inhibiting CLPP1 expression.

The polypeptide of Invention II is patentably distinct from the antibody of Invention III. Invention II is drawn to an isolated polypeptide that can be used to screen for modulators of activity. Invention III is drawn to an antibodies specific for said polypeptide. The antibody can be used to detect protein. The polypeptide and the antibody have different structures, functions and mechanisms of action. The Inventions are classified differently. It would require undue burden to search the isolated polypeptide with the antibody.

The polypeptide of Invention II and the transgenic animals of each of Inventions IV and V are patentably distinct. The polypeptide and the animal are functionally and structurally distinct and have different purpose and different modes of action. The polypeptide of Invention II can be used in vitro to make antibody. The animals of Inventions IV and V can be used to screen test compounds. The inventions are classified differently. It would require an undue burden to search Invention II with either of Inventions IV or V.

Inventions II and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product

as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide can be used to screen for activity modulators or to make antibodies.

Inventions II and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide can be used to screen for binding agents or to make antibodies.

The polypeptide of Invention II is patentably distinct from the pharmaceutical of Invention VIII. In the instant case the polypeptide of Invention II is structurally and functionally distinct from the pharmaceutical comprising a functional regulator of a CLPP1 polypeptide. The isolated polypeptide comprises phosphodiesterase activity while the pharmaceutical is not necessarily a polypeptide and it modulates phosphodiesterase activity. The polypeptide can be used to make antibody and is not necessary for the pharmaceutical. The Inventions are classified differently. It would require undue burden to search the isolated polypeptide with the pharmaceutical.

The polypeptide of Invention II and the polynucleotides of Invention IX are patentably distinct. The polypeptide and the polynucleotides are structurally and functionally distinct. The polypeptide of Invention II has CLPP1 activity. The polynucleotide of Invention IX inhibits CLPP1. The structure, function and mode of action of the polypeptide and the polynucleotides

are different. It would require undue burden to search the polypeptide with CLPP1activity with a polynucleotide capable of inhibiting CLPP1 expression.

The antibody of Invention III and the transgenic animals of each of Inventions IV and V are patentably distinct. The antibody and the animals are functionally and structurally distinct and have different purpose and different modes of action. The antibody of Invention III can be used to detect protein. The animals of Inventions IV and V can be used to screen test compounds. The inventions are classified differently. It would require an undue burden to search Invention III with either of Inventions IV or V.

Inventions III and VI are patentably distinct. Invention III is drawn to an antibody that binds CLPP1. The method of Invention VI is drawn to a method of detecting binding of an agent with CLPP1 that does not require the antibody of Invention III. The antibody can be used in different methods such as detection of native, unbound CLPP1. The antibody and the method are classified differently. It would require an undue burden to search Invention III with Invention VI.

Inventions III and VII are patentably distinct. Invention III is drawn to an antibody that binds CLPP1. The method of Invention VI is drawn to a method of screening for agents that modulate CLPP1 activity that does not use or require the antibody of Invention III. The antibody can be used in different methods such as detection of native, unbound CLPP1. The antibody and the method are classified differently and have different purpose. It would require an undue burden to search Invention III with Invention VII.

The antibody of Invention III is patentably distinct from the pharmaceutical of Invention VIII. In the instant case the antibody of Invention III is structurally and functionally distinct from the pharmaceutical comprising a functional regulator of a CLPP1 polypeptide. The antibody

binds to CLPP1 and does not necessarily modulate its activity. The antibody has uses such as detecting protein that do not require the pharmaceutical. The antibody and the pharmaceutical are not necessary one for the other. The Inventions are classified differently. It would require undue burden to search the antibody with the pharmaceutical.

The antibody of Invention III and the polynucleotides that inhibit CLPP1 of Invention IX are patentably distinct. The antibody and the polynucleotides are structurally and functionally distinct. The antibody of Invention III binds to and detects the presence of CLPP1. The polynucleotide of Invention IX inhibits CLPP1. The structure, function and mode of action of the antibody and the polynucleotides are different. It would require undue burden to search the antibody with a polynucleotide capable of inhibiting CLPP1 expression.

The transgenic animals of Inventions IV and V are patentably distinct. The animal of Invention comprises an exogenous nucleic acid encoding CLPP1. The animal of Invention V comprise a nucleic acid that disrupts the endogenous CLPP1 gene. Thus, the animals are structurally different and differ in the amount of CLPP1 present in the animal. It would require undue burden to search the different animals together.

Inventions IV and V are each patentably distinct from the in vitro methods of Inventions VI and VIII. The methods of Inventions VI and VII are drawn to in vitro assays of agents that bind or modulate CLPP1 that do not use or require the transgenic animals. The animals and the in vitro methods are classified differently. It would require undue burden to search the animals together with the methods.

The transgenic animals of Inventions IV and V are patentably distinct from the pharmaceutical of Invention VIII. In the instant case, the animals of Inventions IV and V are

structurally and functionally distinct from the pharmaceutical comprising a functional regulator of a CLPP1 polypeptide. Inventions IV and V are animals with altered levels of CLPP1 activity as a result of genetic modification and have use in screening assays, determining gene function and determining in vivo gene expression profiles. The pharmaceutical is used to treat disease. The Inventions are classified differently. It would require undue burden to search the animals with the pharmaceutical.

The transgenic animals of Inventions IV and V and the polynucleotides that inhibit CLPP1 of Invention IX are patentably distinct. The animals and the polynucleotides are structurally and functionally different. Inventions IV and V are animals with altered levels of CLPP1 activity as a result of a polynucleotide that encodes CLPP1 or disruption of the endogenous CLPP1 gene. The polynucleotide of Invention IX inhibits CLPP1 through a different mode of action than that of Invention V. Thus, structure, function and mode of action of the animals and the polynucleotides are different. It would require undue burden to search the animals with a polynucleotide capable of inhibiting CLPP1 expression.

The methods of each of inventions VI and VII are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. Invention VI is drawn to detecting a CLPP1 binding agent. Invention VII is drawn to detecting agents that modulate CLPP1 activity. It would require undue burden to search Inventions VI and VII together.

The methods of Invention VI and the pharmaceutical of Invention VIII are patentably distinct. Invention VI is drawn to screening for binding agents of CLPP1 that do not require the

pharmaceutical of Invention VIII. The pharmaceutical is used to treat disease and does not require the method of screening for CLPP1 binding agents. The inventions are classified differently. It would require undue burden to search Inventions VI and VIII together.

The methods of Invention VI and the polynucleotides of Invention IX are patentably distinct. Invention VI is drawn to screening for binding agents of CLPP1 that do not require the inhibitory polynucleotides of Invention IX. The inhibitory polynucleotides act through RNA interference to inhibit CLPP1 expression whereas the method of Invention VI works through detecting agent binding to a CLPP1 polypeptide. Thus, the inventions are structurally and functionally different and act through different modes of action. The inventions are classified differently. It would require undue burden to search Inventions VI and IX together.

The methods of Invention VII and the pharmaceutical of Invention VIII are patentably distinct. Invention VII is drawn to screening for modulatory agents of CLPP1 that do not require the pharmaceutical of Invention VIII. The pharmaceutical is used to treat disease and does not require the method of screening as the pharmaceutical can be identified through other mechanisms. The inventions are classified differently. It would require undue burden to search Inventions VII and VIII together.

The methods of Invention VII and the polynucleotides of Invention IX are patentably distinct. Invention VII is drawn to screening for functional modulating agents of CLPP1 that do not require the inhibitory polynucleotides of Invention IX. The inhibitory polynucleotides act through RNA interference to inhibit CLPP1 expression whereas the method of Invention VII works through detecting agents that affect CLPP1 polypeptide activity. Thus, the inventions are structurally and functionally different and act through different modes of action. The inventions

are classified differently. It would require undue burden to search Inventions VII and IX together.

The pharmaceutical and method of disease treatment using a modulator of CLPP1 and the polynucleotides that inhibit CLPP1 expression of Invention IX are patentably distinct. The pharmaceutical and method of treatment do not require the antisense polynucleotides of Invention IX. The pharmaceutical and treatment methods could be carried out using functional modulators such as interacting proteins and CLPP1 binding agents. The inventions are classified differently. It would require undue burden to search Inventions VIII and IX together.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully

examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

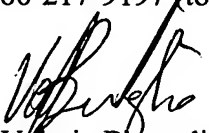
Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Valarie Bertoglio
Examiner
Art Unit 1632